

AWARD NUMBER: W81XWH-16-1-0051

TITLE: Joint Loads and Cartilage Stress in Intact Joints of Military Transtibial Amputees: Enhancing Quality of Life

PRINCIPAL INVESTIGATOR: Dr. Stephen M. Klisch

CONTRACTING ORGANIZATION: California Polytechnic State University
San Luis Obispo, CA 93407

REPORT DATE: April 2017

TYPE OF REPORT: ANNUAL

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE April 2017		2. REPORT TYPE ANNUAL		3. DATES COVERED 15Mar2016 - 14Mar2017	
4. TITLE AND SUBTITLE Joint Loads and Cartilage Stress in Intact Joints of Military Transtibial Amputees: Enhancing Quality of Life				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER W81XWH-16-1-0051	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Stephen M. Klisch, Ph.D. E-Mail: sklisch@calpoly.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) California Polytechnic State University San Luis Obispo, CA 93407				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT The goals of this project are to identify exercises that maintain intact limb knee and hip joint and cartilage tissue loads at safe levels and, consequently, enhance the quality of life (QoL) via prevention of intact limb joint arthritis for military transtibial amputees. Progress during year 1 includes the following. 1) Purchased, installed, and developed protocols for instrumentation needed for motion analysis studies. 2) Tested eight out of 20 subjects in gait, cycling, and elliptical training experiments. 3) Developed analytical methods to obtain accurate knee joint kinematics (while minimizing errors due to soft tissue artifact and crosstalk); analysis of tested subjects underway. 4) Developed analytical methods to obtain knee joint loads using EMG-driven inverse dynamics; analysis of tested subjects underway. 5) Conducted five knee MRI scans and commenced finite element model development. At the end of year 1, results and findings are preliminary and not available; however, several conference papers are being prepared for submission in the next quarter.					
15. SUBJECT TERMS Amputee, prosthesis, knee, hip, biomechanics, cartilage, arthritis, finite element analysis					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 12	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U			19b. TELEPHONE NUMBER (include area code)

Table of Contents

	<u>Page</u>
1. Introduction.....	1
2. Keywords.....	1
3. Accomplishments.....	1
4. Impact.....	4
5. Changes/Problems.....	5
6. Products.....	6
7. Participants & Other Collaborating Organizations.....	7
8. Special Reporting Requirements.....	9
9. Appendices.....	N/A

1. INTRODUCTION: Abnormal biomechanics is a risk factor for knee joint osteoarthritis (OA) and is likely related to joint pain and OA among transtibial amputees. Although lower limb joint loading during gait for patients with high risk for OA has been examined, there are a lack of studies on joint loading for other fitness sustainment exercises and on predicting cartilage tissue loads of lower limb prosthesis users. The goals are to identify exercises that maintain intact limb knee and hip joint and cartilage tissue loads at safe levels and, consequently, enhance the quality of life (QoL) via prevention of intact limb joint OA for military transtibial amputees. The overall hypothesis is that intact limb joint and cartilage tissue loads depend on disability status (amputee vs. control) and exercise type (walking vs. cycling vs. elliptical training). Specific Aim 1 is to conduct motion analysis experiments and calculate intact limb knee and hip joint loads in amputee and control group subjects. Specific Aim 2 is to develop and use subject-specific finite element models to calculate intact limb knee joint cartilage loads in amputee and control group subjects.

2. KEYWORDS: Amputee, prosthesis, knee, hip, biomechanics, cartilage, arthritis, finite element analysis

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Objective 1: Calculate knee and hip joint loads for walking, cycling, and elliptical training exercises.

Task 1.1: Recruitment of n=10 amputee and n=10 control group subjects. Target date: 1/13/2018. Completion %: 45.

Task 1.2: Motion analysis experiments with amputee and control group subjects. Target date: 1/13/2018. Completion %: 40.

Task 1.3: EMG-driven inverse dynamic (ID) analyses with OpenSim for amputee and control group subjects. Target date: 1/13/2019. Completion %: 25.

Task 1.4: Statistical analyses of knee and hip joint contact resultants for amputee and control group subjects. Target date: 1/13/2019. Completion %: 5.

Objective 2: Calculate knee joint cartilage tissue loads for walking, cycling, and elliptical training exercises.

Task 2.1: Conduct MRI scans of intact limb knee joints of n=10 amputee and n=10 control group subjects. Target date: 1/13/2018. Completion %: 25.

Task 2.2: Develop solid models of the intact limb knee joints for amputee and control group subjects. Target date: 1/13/2019. Completion %: 15.

Task 2.3: Develop FE models of the intact limb knee joints for amputee and control group subjects. Target date: 1/13/2019. Completion %: 5.

Task 2.4: Conduct FE model simulations for amputee and control group subjects. Target date: 1/13/2019. Completion %: 0.

Task 2.5: Statistical analyses of knee joint cartilage tissue loads for amputee and control group subjects. Target date: 1/13/2019. Completion %: 0.

What was accomplished under these goals?

Major activities.

Hiring students. A total of nine student research assistants were hired and trained.

Equipment. Equipment items (EMG system, extra walkway sections and force plate for gait analysis, elliptical trainer, load cells for elliptical trainer, motion capture cameras) were purchased, installed, and used in experiments. Protocols were developed for equipment use. All motion capture cameras were re-positioned and calibrated in order to improve the quality of motion capture data.

Soft tissue artifact (STA) compensation. We completed development of a state-of-the-art analytical technique to reduce STA-induced errors in measured anatomical knee angles during motion analysis. The analysis models a body segment as a pseudo-rigid body (PRB) i.e. a body that experiences only homogeneous deformations.

Specific tasks included the following. 1) Developed and optimized custom software (MATLAB) in order to analyze gait for both the left and right legs. 2) Optimized post processing procedures in software through the restructuring of the data analysis architecture. 3) Integrated Principal Component Analysis (PCA) into the post-processing procedure. 4) Reorganized analysis software by combining the code for gait, bike, and elliptical into a single master file. 5) Wrote new software to post process bike and elliptical experimental data. 6) Developed protocols and software to conduct further validation studies in order to compare PRB method results to a state of the art rigid-body optimization method, the Procrustes Solution (PS), which picks an optimized rigid body rotation tensor using Single Value Decomposition (SVD) for a cluster of n-markers.

Crosstalk error compensation. We completed development of a state-of-the-art analytical technique to reduce crosstalk errors in measured anatomical knee angles during motion analysis using a statistical technique employing linear algebra call Principal Component Analysis (PCA).

Specific tasks included the following. 1) Data for 6 subjects were gathered and processed in Cortex. 2) Custom software (MATLAB) was developed to use PCA to minimize flexion-adduction correlation R^2 values (considered a quantitative measure of crosstalk error) and, thus, produce corrected knee angles. 3) An algorithm and code has been completed to determine the PCA-corrected flexion and adduction axes. 4) Analysis completed for 1 subject: MATLAB code reduces R^2 values between flexion-adduction angles, used to measure crosstalk, to zero for data taken from 1 gait and 1 cycling trial.

Experiments. Specific tasks included recruiting and testing 6 control group and 2 amputee group subjects in gait, cycling, and elliptical training. Recruitment of additional subjects is underway.

EMG-driven ID analyses. We completed development of our OpenSim protocols. Specific tasks included the following. 1) Learned how to represent load cell output as point forces, and techniques to filter load cell data to reduce residuals in OpenSim's Residual Reduction Algorithm. 2) Finalized a method to time sync EMG and motion capture data. 3) Analysis of control group subject data is underway; we have successfully ran a complete analysis using kinematics, kinetics, and EMG data for one subject's gait. 4) Considerable progress was made towards refining the cycling protocol. Running OpenSim with cycling kinematics and only pedal forces produces pelvic residuals that are added to the model in order to match the sum of the

forces with the mass and accelerations using Newton's second law. These residuals were compared (favorably) to published values to validate OpenSim results.

Conduct MRI scans. MRI scans have been completed for 5 of the 8 subjects tested to date.

Develop solid knee models using MRI scans. Specific tasks included the following. 1) Wrote MATLAB script to remove any personally identifying information from received MRI scans. 2) A custom image processing script was developed to adjust MRI contrast to optimal values and filter out a slight degree of image noise. The test MRI sequence was successfully segmented and smoothed into a 3-D whole knee joint model. The medial and lateral meniscus, medial and lateral tibial cartilage, femoral cartilage, and patellar cartilage were evaluated for volumetric accuracy against published statistical data. 3) Segmented patient MRI scans as they were received. Currently, 3 knees have been segmented with 3 more de-identified and preprocessed.

Develop FE knee models using MRI scans. Specific tasks included the following. 1) Wrote a processing script in MATLAB with the use of The Geometry and Image-Based Bioengineering add-On for MATLAB (GIBBON) that generates a 3D volume mesh from the .stl surface mesh for each body and creates an FEBio input file. Importing this file into FEBio's PreView program presents a 3D view of the entire FE model and allows the input of boundary constraints/loading and node set definition. 2) Commenced finite element mesh generation of developed solid models.

Specific objectives.

Objective 1. Calculate knee and hip joint loads for walking, cycling, and elliptical training exercises.

Task 1.1. (recruitment). Recruitment of 6 control and 2 amputee subjects completed. Recruitment of additional subjects underway.

Task 1.2. (experiments). Experiments with 6 control and 2 amputee subjects completed. Data inspection reveals that all experiments produced useable data.

Task 1.3. (ID analyses). PRB & PCA analysis with all tested subjects' data is underway. Meanwhile, using the non-corrected data, EMG-driven OpenSim analyses are underway (results are pending).

Task 1.4. (statistics). Nothing to report.

Objective 2. Calculate knee joint cartilage tissue loads for walking, cycling, and elliptical training exercises.

Task 2.1. (MRI scans). MRI scans have been completed for 5 of the 8 subjects tested to date. MRIs are currently being scheduled for the other 3 tested subjects.

Task 2.2. (develop knee solid models). Currently, 3 knees have been segmented with 3 more de-identified and preprocessed.

Task 2.3. (develop knee FE models). Finite element model development is nearing completion for 1 subject.

Task 2.4. (finite element analysis). No progress has been made.

Task 2.5. (statistics). Nothing to report.

Significant results.

Final results have been (or are being generated) for the 8 tested subjects in the following categories: ground-reaction and pedal forces, anatomical knee angles corrected for STA and crosstalk, knee contact loads predicted by EMG-driven inverse dynamics. Two-three conference papers are being prepared for submission in February 2017.

Other achievements.

None to report.

Stated goals not met.

1) In our last quarterly report, we stated the intent to test 4 more amputee subjects. To date, we have tested only n=2 amputee subjects, so we are behind schedule for amputee subjects.

What opportunities for training and professional development has the project provided?

Training activities.

Training: protection of human subjects. A total of 7 students completed on-line CitiProgram training (course: Biomedical Researcher: Basic/Refresher) on protection of human subjects in research.

Miscellaneous. The research is being primarily conducted by B.S. and M.S. level students. Students were training by faculty mentors on motion analysis experiments and analysis and general safety procedures throughout the period of report. Also, students were trained in CPR.

Professional development.

OpenSim Virtual Workshop. In October 2016, 6 students participated in the OpenSim virtual workshop for 1 week. In order to participate, the students presented a proposal before the workshop began and then submitted a summary slide after the workshop concluded. Goals included learning how to better use OpenSim for the required EMG-driven inverse dynamic analyses.

How were the results disseminated to communities of interest?

Nothing to report; results are still too preliminary for dissemination.

What do you plan to do during the next reporting period to accomplish the goals?

- 1) Recruit and test 2 more amputee and 2 more control group subjects.
- 2) Perform STA and crosstalk correction on all subjects.
- 3) Perform EMG-driven OpenSim analysis on all subjects.
- 4) FEA analysis: continue model development from MRIs.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

The experimental and analysis results are still too preliminary to comment on their impact. However, the state-of-the-art PRB and PCA methods developed for minimizing errors due soft tissue artifact and crosstalk, respectively, will impact the field of motion analysis and relatively few groups have used and published similar methods. This impact will be to improve estimates

of knee biomechanics and, consequently, interventions aimed at normalizing biomechanics, reducing injury, and, ultimately, increasing QoL.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report; as results become finalized, this section will be updated as the societal impacts include recommendations for lifelong fitness sustainment exercises that maintain healthy knee loads for transtibial amputees.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Actual or anticipated problems or delays and actions or plans to resolve them

We are experiencing difficulty, likely due to our rural location, in identifying amputee subjects that meet all of our inclusion/exclusion criteria. Originally, the inclusion/exclusion criteria was quite severe in an effort to obtain subjects that would be expected to have normal biomechanics in their intact leg while being eligible for MRI tests. Further, as we suggested in our original proposal, development of the knee FEA models has taken considerable time. In our original proposal, we clearly stated that it would be difficult to develop knee FEA models for all 20 subjects and thus proposed an alternate plan of developing knee FEA models for only 6 subjects.

To deal with these problems, the following actions have been undertaken or are proposed.

1) We will restrict our targeted number of MRI models to 6; thus, we have already modified our IRB protocol (and obtained Cal Poly IRB approval) so that the inclusion/exclusion criteria for MRI scans is only applicable for subjects whom will receive a follow-up MRI (e.g. implanted pacemakers and hardware are complications that have excluded subjects from the study solely due to MRI safety). 2) We have already obtained Cal Poly's IRB approval to increase the maximum age of subjects from 40 to 50 years. This change was not considered to increase risk to human subjects so only Cal Poly IRB approval was needed. 3) We have already obtained Cal Poly's IRB approval to increase the maximum years since amputation surgery from 10 to 15 years. This change was not considered to increase risk to human subjects so only Cal Poly IRB approval was needed. 4) We are considering modifying our budget and protocol so that we can house subjects that will be recruited from outside of our local community. If we decide to move in this direction, no changes will be made until proper IRB approval is granted.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Please see above for the rationale for the following changes. 1) We will restrict our targeted number of MRI models to 6; thus, we have already modified our IRB protocol (and obtained Cal

Poly IRB approval) so that the inclusion/exclusion criteria for MRI scans is only applicable for subjects whom will receive a follow-up MRI (e.g. implanted pacemakers and hardware are complications that have excluded subjects from the study solely due to MRI safety). 2) We have already obtained Cal Poly's IRB approval to increase the maximum age of subjects from 40 to 50 years. This change was not considered to increase risk to human subjects so only Cal Poly IRB approval was needed. 3) We have already obtained Cal Poly's IRB approval to increase the maximum years since amputation surgery from 10 to 15 years. This change was not considered to increase risk to human subjects so only Cal Poly IRB approval was needed. 4) We are considering modifying our budget and protocol so that we can house subjects that will be recruited from outside of our local community. If we decide to move in this direction, no changes will be made until proper IRB approval is granted.

Significant changes in use or care of vertebrate animals.

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

- Journal publications.**

- Nothing to report.

- Books or other non-periodical, one-time publications.**

- Nothing to report.

- Other publications, conference papers, and presentations.**

- Nothing to report.

- **Website(s) or other Internet site(s)**

- Nothing to report.

- **Technologies or techniques**

- Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.*

- Nothing to report (see "other products" below).

- **Inventions, patent applications, and/or licenses**

- Nothing to report.

- **Other Products**

- 1) Custom PRB method software (MATLAB) to reduce STA for gait, cycling, and elliptical experiments. Related protocol in progress.
 - 2) Custom SVD method software (MATLAB). Related protocol in progress.
 - 3) Custom PCA software (MATLAB) to reduce crosstalk error for gait, cycling, and elliptical experiments. Related protocol in progress.

- 4) Custom PCA software (MATLAB) to determine the PCA-corrected knee flexion and adduction axes.
- 5) Custom time sync code (MATLAB) to time sync EMG and motion capture data.
- 6) MATLAB script that de-identifies MRI scans to preserve patient privacy.
- 7) MATLAB script utilizing GIBBON to turn .stl surface meshes into tetrahedral computational meshes and write FEBio input files.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

Name: Stephen Klisch
Project Role: PI
Nearest person month worked: 3
Contribution to Project: Dr. Klisch managed the project.
Funding Support: Dr. Klisch is also funded by Cal Poly's Donald E. Bently Center for Engineering Innovation.

Name: Scott Hazelwood
Project Role: co-PI
Nearest person month worked: 2
Contribution to Project: Dr. Hazelwood managed the finite element related project aims.
Funding Support: Dr. Hazelwood is also funded by Cal Poly's sabbatical program for Professors.

Name: Nina Yadlowsky
Project Role: Undergraduate student
Nearest person month worked: 4
Contribution to Project: Developed protocols & software for accurately measuring knee kinematics. Conducted experiments and data analysis.

Name: Alejandro Gonzalez-Smith
Project Role: Graduate student
Nearest person month worked: 4
Contribution to Project: Developed protocols & software for accurately measuring knee kinematics. Conducted experiments and data analysis.

Name: Jordan Skaro
Project Role: Undergraduate student
Nearest person month worked: 3
Contribution to Project: Developed protocols & software for accurately measuring knee kinematics. Conducted experiments and data analysis.

Name: Greg Orekhov
Project Role: Undergraduate Student
Nearest person month worked: 5

Contribution to Project: Purchased and installed equipment. Developed protocols for conducted EMG-driven inverse dynamic analyses of knee joint loads. Conducted experiments and data analysis.

Name: Samuel Tucker

Project Role: Undergraduate Student

Nearest person month worked: 3

Contribution to Project: Developed protocols & software for accurately measuring knee kinematics. Conducted experiments and data analysis.

Funding Support: Mr. Tucker is also funded by Cal Poly's Human Motion Biomechanics Lab account (accrued with gifts/donations) and a W.M. Keck Foundation grant.

Name: Megan Pottinger

Project Role: Undergraduate Student

Nearest person month worked: 4

Contribution to Project: Purchased and installed equipment. Developed protocols for conducted EMG-driven inverse dynamic analyses of knee joint loads. Conducted experiments and data analysis.

Funding Support: Ms. Pottinger is also funded by a W.M. Keck Foundation grant.

Name: Katherine Mavrommati

Project Role: Undergraduate Student

Nearest person month worked: 4

Contribution to Project: Purchased and installed equipment. Developed protocols for conducted EMG-driven inverse dynamic analyses of knee joint loads. Conducted experiments and data analysis.

Funding Support: Ms. Mavrommati is also funded by a W.M. Keck Foundation grant.

Name: Michael Rumery

Project Role: Graduate Student

Nearest person month worked: 5

Contribution to Project: Developed protocols for development of finite element models and analyses. Conducting finite element analyses.

Name: Greg Lane

Project Role: Undergraduate Student

Nearest person month worked: 3

Contribution to Project: Developed protocols for development of finite element models and analyses. Conducting finite element analyses.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Dr. Saikat Pal, formerly a Professor in Cal Poly's Biomedical Engineering Department, left our University in September 2016. In the original budget, Dr. Pal was awarded \$14,735 in direct pay to assist with the finite element modeling efforts. That work will now be completely managed by Dr. Scott Hazelwood and there are no anticipated problems with this change. The budget will be revised and the funds will be shifted to pay for student researchers and/or Dr. Hazelwood.

What other organizations were involved as partners?

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

Nothing to report.

9. APPENDICES:

Nothing to report.